Citation:

Johnston CS, Tjonn SL, Swan PD, White A, Hutchins H, Sears B. Ketogenic low-carbohydrate diets have no metabolic advantage over nonketogenic low-carbohydrate diets. *Am J Clin Nutr.* 2006 May;83(5):1055-61.

PubMed ID: 16685046

Study Design:

Randomized Clinical Trial

Class:

A - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To compare weight loss and the metabolic effects of a ketogenic low-carbohydrate diet (KLC) and of a nonketogenic, low-fat low-carbohydrate diet (NLC).

Inclusion Criteria:

- Sedentary, overweight men and women
- Age 20 - 60 y
- BMI > 25

Exclusion Criteria:

- Diagnosed disease
- Use of prescription medications

Description of Study Protocol:

Recruitment

Recruitment methods not described.

Design: Randomized clinical trial

Blinding used (if applicable): implied with measurements

Intervention (if applicable)

- Ketogenic low-carbohydrate diet (KLC) or low-fat, non-ketogenic low-carbohydrate diet (NLC) for 6 wks.

Statistical Analysis

- The repeated-measures analysis of variance to assess differences in metabolic data.
- To assess change in body mass at week 6, an unpaired Student's *t* test was performed.
- Power calculations did indicate a 70% power to detect a change of 0.6 mmol/L in LDL cholesterol.
- Pearson's correlation was used to identify relations between variables.
- Significance at $P \leq 0.05$.

Data Collection Summary:

Timing of Measurements

- Body weight, fat mass, hunger assessment, and Profile of Mood States (POMS): day 1 of each week
- Body weight and fat mass again at week 10 after the 4-wk self-monitored diet adherence.
- 24-h urine sample, fasting bloods, and resting energy expenditure (REE): baseline and weeks 2 and 6

Dependent Variables

- REE (MAX-2 metabolic cart after 12-h fast and 24-h avoidance of light-to-heavy activity)
- Glucose; creatinine; total, HDL and LDL cholesterol and triacylglycerols (standard lab)
- Plasma insulin (radioimmunoassay)
- Insulin sensitivity (homeostasis model assessment [HOMA] index)
- Urinary creatinine (colorimetric procedures)
- Plasma uric acid, C-reactive protein, liver enzymes and urinary calcium (standard lab)
- Blood β-hydroxybutyrate (enzymatically)
- Fatty acid composition (gas chromatography)
- Body weight and Fat mass (Tanita Body Composition Analyzer TBF-300A)
- Hunger ratings (7-point Likert scale:extremely hungry to extremely full)
- Mood state (POMS questionnaire)

Independent Variables

- Diets were provided to participants for 6 wks at the test site Monday through Friday and packaged to take home for the weekends. After the 6-wk trial, a registered dietitian counseled the participants on the diet details and provided meal plans and recipes for the remaining 4 weeks of the study.
- KLC diet: 60% fat, 21% SFA, 9% CHO, 33% PRO
- NLC diet: 30% fat, 9% SFA, 42% CHO, 31% PRO

Control Variables

- Protein content of diets, multivitamin supplement, and calories at 70% of weight maintaining need.

Description of Actual Data Sample:

Initial N: 20 (4 men, 17 women, 1 unknown)

Attrition (final N): 19 (KLC diet: 2 men, 7 women; NLC diet: 2 men, 8 women)

Age: KLC group: 38.4 ± 3.9 years; NLC group: 37.2 ± 3.9 years

Ethnicity: Not described

Other relevant demographics:

Anthropometrics No significant differences in weight, fat mass, BMI, percent body fat, waist circumference, waist:hip ratio, blood lipids or fasting glucose and insulin.

Location: Arizona

Summary of Results:

Key Findings:

- There were no significant differences in weight loss, fat mass reduction, or change in fat-free mass between the two diet groups.
- Insulin resistance decreased in both diet groups.
- LDL concentrations increased in 5 KLC dieters and decreased in 4 KLC dieters while it increased in 2 NLC dieters and decreased in 8 NLC dieters.
- Feelings of vigor-activity were significantly greater for NLC compared with KLC.
- Hunger ratings improved over the 6-wk trial in both groups and were not significantly different between the groups.

Variables	KLC Group Measures and confidence intervals	NLC group Measures and confidence intervals	Statistical Significance of Group Difference
Weight loss (kg)	6.3 ± 0.6	7.2 ± 0.8	$P = 0.324$
Fat mass (kg)	3.4	5.5	$P = 0.111$
AA:EPA*	39.2 ± 7.8	20.9 ± 2.9	$P = 0.038$

*Arachidonic acid: eicosapentaenoic acid

Other Findings

- HDL cholesterol fell 9% in both diet groups.
- Weight-adjusted REE and fat oxidation increased for both groups.
- LDL cholesterol was directly correlated with blood β-hydroxybutyrate concentrations ($r = 0.297$, $P = 0.025$)
- Serum γ-glutamyltransferase concentrations fell in both groups. C-reactive protein, 24-h urine calcium concentrations were not significantly affected by either diet. Creatinine clearance and plasma uric acid concentrations were below baseline values for both groups.

Author Conclusion:

The KLC diets did not offer any significant metabolic advantage over the NLC diet. Both diets

were effective at reducing total body mass and insulin resistance, but blood ketones were directly related to LDL-cholesterol concentrations and inflammatory risk was elevated with adherence to the KLC diet. The NLC diet was associated with feelings of high energy.

Reviewer Comments:

Small numbers of subjects in groups. Study duration only 6 weeks long. Although the abstract stated that the participants were sedentary, there was no documentation of controlling the physical activity.

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	Yes
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	Yes

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes

2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	No
3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	Yes
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	Yes
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	N/A
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	Yes
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	Yes
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	No
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	Yes
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	N/A

5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes
6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	Yes
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	???
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	No
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	Yes
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	N/A
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes

	8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
	8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
	8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A
	8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	N/A
	8.6.	Was clinical significance as well as statistical significance reported?	Yes
	8.7.	If negative findings, was a power calculation reported to address type 2 error?	No
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**		Yes
	9.1.	Is there a discussion of findings?	Yes
	9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**		Yes
	10.1.	Were sources of funding and investigators' affiliations described?	Yes
	10.2.	Was the study free from apparent conflict of interest?	Yes